REMARKS

Status of Claims

Prior to entry of this amendment, claims 19 and 23-36 were pending. Claims 25-33 are cancelled and claims 23-24 are amended herein. No new matter is added.

Objections to the Title and Abstract

The title and abstract were objected to as not accurately describing the claimed invention. The title and abstract are amended herein as requested by the Examiner.

Claim rejections

35 U.S.C. § 112, Second Paragraph

Claims 28 and 33 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting a vaccine comprising 8 consecutive amino acids of SEQ ID NO:4, which is 7 amino acids long. Applicants note that the cancellation of these claims renders this rejection moot. Accordingly, Applicants request withdrawal of the rejection on this basis.

35 U.S.C. § 112, First Paragraph

Claims 19 and 23-33 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled. The Examiner asserts "that it is unlikely that the claimed peptides could function as effective vaccines nor is it likely that they could even be bound by antibodies in diagnostic assays as broadly claimed." OA, at p. 3.

In particular, the Examiner states that "[t]he peptides are claimed only as vaccines. While a complete demonstration of efficacy is not required, some demonstration, or at least sound scientific reasoning is required for a finding of enablement. In this instance the specification discloses only that, 'three CDR3-encoded sequences were detected in high percentage of MS-derived specimens as opposed to control specimens" . . . Curiously, it is not disclosed what the 'high percentage' actually was." Id., at p. 4. Applicants respectfully assert that use of the peptides as claimed is based on sound scientific reasoning. In particular, use of the peptides as vaccines is based on the surprising finding that a majority of MS patients have T cell receptors

comprising the sequence of SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6. In contrast, less than a third of healthy patients have T cells receptors comprising the sequence of SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6.

Table 2 indicates SEQ ID NO:4 (Genbank Accession MS2002-DH) is found in 57.5% of the samples taken from MS patients. Specification, at Table 2. In contrast, SEQ ID NO:4 is found in only 33% of the samples taken from healthy patients. Id. As stated in the specification, "The results in Table 2 are surprising, because a number of studies do not support the preferential use of particular Vβ-Dβ-Jβ gene products. . . It was generally believed in the art that the heterogeneity of Vβ-Dβ-Jβ gene usage would significantly impair the feasibility of using a peptide vaccine . . . The results herein describe for the first time that a vaccine based on one or more peptides may prove beneficial in the elimination of pathogenic autoreactive T cells." The ordinarily skilled artisan recognizes that TCR peptides associated with an autoimmune disease may be used as a vaccine in the treatment of the autoimmune disease. *See, e.g.*, Vandenbark *et al.*, *Nat. Med.* 10:1109 (1996); Zang *et al.*, *Int'l Immunol.* 15:1073-1080 (2003).

The Examiner also states that with regard to vaccines, in order to function in that capacity the peptides must be bound and presented by MHC class II, and that the minimum length of a peptide for MHC class II binding is twelve amino acids. Action at p. 4 (citing Godkins et al. (2001)). Applicants respectfully disagree that the claimed peptides must be of 12 amino acids in length in order to generate the anti-idiotypic immune response contemplated and described in the instant specification. In fact, the Godkin reference upon which the Examiner relies does not support the Examiner's absolute proposition of peptide length. Rather, as explained in the accompanying declaration from Dr. David Fitzpatrick, the core peptide region necessary for MHC binding and presentation in Godkin was only nine amino acids in length, with the unbound flanking regions of the peptide independent of MHC-peptide binding. Fitzpatrick Declaration, at ¶ 7.

As described for the first time by Applicants, TCR peptides comprising the sequence of SEQ ID NO:4 are found in a majority of patients with multiple sclerosis. Accordingly, such peptides may be used as vaccines to generate an anti-idiotypic immune response, which may include either or both T and B cell responses. " See, id., at ¶ [0017]. As explained and attested to by Dr. Fitzpatrick, the skilled artisan would

readily recognize that peptides 7-8 amino acids in length can generate the requisite anti-idiotypic immune response. Indeed, Applicants' own earlier work demonstrates that an 8-mer TCR peptide readily induces an anti-idiotypic T cell response. Zang (2003), *supra*. Further, it is also well known and well-established that antibody responses may be raised against peptides of as few as five (5) amino acids and, in fact, many commercially available antibodies are generated against peptides that are less than twelve (12) amino acids in length. *See* Fitzpatrick Declaration, ¶5. Accordingly, and contrary to the Examiner's suggestion, the skilled artisan would readily recognize that Applicants' peptides are adequate to induce an anti-idiotypic immune response as presently claimed.

In light of the above remarks, Applicant respectfully asserts that the invention as presently claimed is fully enabled. Accordingly, withdrawal of the rejections on this basis is respectfully requested.

35 U.S.C. § 112, First Paragraph

Claims 25-28 and 30-33 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants note that the cancellation of these claims renders this rejection moot. Accordingly, Applicants request withdrawal of the rejection on this basis.

35 U.S.C. § 102(b) -- Anticipation

Claims 24, 25, 29, and 30 are rejected under 35 U.S.C. § 102 as allegedly anticipated by PCT Publication No. WO 01/42277. The Examiner contends that WO 01/42277 teaches a peptide of between 4 and 20 amino acids in length comprising 5 consecutive amino acids of SEQ ID NO:4. OA, at p. 5 (citing SEQ ID NO:885).

Independent claims 19 and 24 as amended herein are directed toward a peptide comprising the sequence of SEQ ID NO:4, i.e., the sequence ASSTDWS. SEQ ID NO:885 of WO 01/42277 has the sequence of AYSNASSTDS. In other words and as acknowledged by the Examiner, SEQ ID NO:885 discloses a peptide comprising only five consecutive amino acids of SEQ ID NO:4. Further, WO 01/42277 does not

five consecutive amino acids of SEQ ID NO:4. Further, WO 01/42277 does not disclose or suggest a peptide comprising the sequence of SEQ ID NO:4. Accordingly, WO 01/42277 cannot anticipate the instant claims because it fails to teach or suggest a peptide comprising the sequence of SEQ ID NO:4.

Having distinguished the independent claims from the art of record, Applicant submit that the claims dependent therefrom are patentable for at least the same reason. However, Applicants reserve the right to separately address the patentability of the dependent claims in the future, should that become necessary.

CONCLUSION

Applicants respectfully submit that the instant application is in condition for allowance. Entry of the amendments and an action passing this case to issue is therefore respectfully requested. In the event that a telephone conference would facilitate examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided. The Commissioner is authorized to charge the requisite extension of time fees along with any other fees due with this response to Deposit Account No: 50-2387 and credit any over payment to the same.

Respectfully submitted,

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